

allowance of the pending claims and do not necessarily acquiesce in the Examiner's determinations.

8. The abstract is objected to as not being descriptive of the invention to which the claims are directed. Applicant has amended the abstract to refer to the subject matter being claimed. Reconsideration and withdrawal of this objection are respectfully requested.

9. The title of the invention is objected to as not being descriptive of the invention to which the claims are directed. Applicant has amended the title to reflect the claimed subject matter. Reconsideration and withdrawal of this objection are respectfully requested.

10. Applicant notes that the application was filed with informal drawings. Applicants will provide formal drawings upon indication of allowable subject matter.

11. Applicant acknowledges that any errors found in the specification will be corrected as discovered.

12. Claim 59 and dependent claims 61-63 are objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form. Applicant has cancelled claim 59, thereby rendering this rejection moot.

13. Claims 64 and 69-70 are objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form. Applicant respectfully points out, however, that the "antibody" of claim 58 can be a labeled antibody or an unlabeled antibody, while the antibody of claim 64 is limited to being a labeled antibody. Accordingly, claim 64 properly narrows the subject matter of claim 58. In addition, Applicants have amended claim 68 to provide proper antecedent basis for the recitation of claim 69. Reconsideration and withdrawal of this objection are respectfully requested.

14. Claims 11, 58, 61, and claims dependent thereon are objected to under 37 C.F.R. § 1.821(d) for not reciting the SEQ ID Nos. in the claims. Applicant respectfully points out that this section does not require that a SEQ ID be present in any and all claims, but only where a specific amino acid or nucleotide sequence is recited in the text of the claim. Applicants have amended these claims to define the recited protein by behavioral characteristics sufficient to

distinguish it from other unrelated proteins. Reconsideration and withdrawal of this objection are respectfully requested.

15. Claim 76 is objected to for reciting "in samples in cells" rather than "in samples of cells." Applicant has cancelled this claim, rendering this rejection moot.

16-17. Claims 64, 68-76, and 82 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants have incorporated by reference material from 08/154,915 that supports the presently claimed invention both as it relates to the originally disclosed sequence, SEQ ID No. 35, and the complete human p16 sequence, SEQ ID No. 2. As the Examiner has indicated that this material provides adequate support for the claimed subject matter, reconsideration and withdrawal of this rejection are respectfully requested.

18. Claims 11, 58, 61-64, 66, 68-70, 72-76, and 79-82 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Solely to expedite prosecution of the remaining claims, Applicants have amended the pending claims to be directed to subject matter disclosed in the priority documents and the present specification (see, for example, the attached priority document at pages 29-30 and the present application at pages 52-53). Applicants reserve the right to prosecute claims of similar or differing scope in subsequent applications. Reconsideration and withdrawal of this rejection are respectfully requested.

19. Claims 11, 58, 61-64, 66, 68-70, 72-76, and 79-82 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Solely to expedite prosecution of the remaining claims, Applicants have amended the pending claims to reflect subject matter that the Examiner has indicated as being adequately supported by the present specification. Applicants have also added new claims directed to subject matter indicated by the Examiner as having adequate written description going all the way back to WO 94/09135 and 08/154,905. Applicants have amended the sequence listing to include the 148-amino acid p16 sequence. Accordingly, Applicants submit that the pending claims comply with the written description requirement. Reconsideration and withdrawal of this rejection are respectfully requested.

20-21. Claims 11, 58, 61-64, 66, 71, and 79-82 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants have amended the pending claims, as discussed above, to recite specific characteristics of the protein, thereby rendering this rejection moot. As can be readily seen from the specification and the priority documents, such as Figure 2 of the priority application attached hereto as Exhibit A, the subject p16 protein is the only protein that meets these claim limitations. Moreover, since an antibody can be prepared without knowing the structure or sequence of the protein antigen, the subject matter as defined is as clear as the subject matter permits. *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81 (Fed.Cir. 1986) (definiteness requirement does not require more precision than the relevant technology permits). Claims 71 and 82 have been cancelled, thereby rendering the rejection moot as applied to these claims. Reconsideration and withdrawal of this rejection are respectfully requested.

22. Applicants gratefully acknowledge that claim 11 is considered to have a priority date at least as early as 11/18/93. Applicants also note that the Examiner has acknowledged that SEQ ID No. 2 of the present application is supported in U.S. 08/248,812, filed May 25, 1994.

23-25. Claims 58-77, 79-80, and 82 are rejected under 35 U.S.C. § 102(e) as being anticipated by Kamb and by Skolnick. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants note that claim 11, granted an earlier priority date by the Examiner as pointed out above, is not rejected over these references, because that priority date precedes the availability of either of these references. Applicants have amended the remaining claims to conform to the Examiner's findings of support in priority applications in order to extend this priority date to all pending claims relating to SEQ ID No. 35, which has support acknowledged by the Examiner at least as early as 11/18/93. Accordingly, Applicants submit that neither Kamb nor Skolnick is available as prior art against the present claims. Reconsideration and withdrawal of this rejection are respectfully requested.

26. Claims 68-70, 72-73, and 76 are rejected under 35 U.S.C. § 102(b) as being anticipated by Busch et al., U.S. Patent No. 4,794,077. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants respectfully submit that claim 68 is directed to antibodies specifically immunoreactive with a 16 kD protein. The Office Action establishes no factual basis for its assumption that such an antibody would inherently bind to p145 as taught by Busch et al. If this rejection is to be maintained, Applicants request that the grounds for this assumption be clarified on the record. Applicants further point out that claim 68 has been amended to define the p16 protein by characteristics not apparently shared by p145. Applicants assert that no basis has been set forth to indicate how or why an antibody that would bind to a protein having the recited characteristics would also bind to the p145 protein taught by Busch et al. Reconsideration and withdrawal of this rejection are respectfully requested.

27-28. Claims 11, 58-77, and 79-82 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Xiong et al. in view of Busch et al. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants direct the Examiner's attention to U.S. Patent Application No. 07/991,997, filed December 17, 1992, a priority document of the present application. As the Examiner has

indicated that this filing has been unavailable for comparison, Applicants provide herewith as Exhibit A a copy of the specification as filed. Pages 29-31 and Figures 2-5 present much of the material disclosed by Xiong et al., and Y. Xiong and D. Beach are listed as inventors. Page 7, lines 14-18, expressly contemplates antibodies that bind to p16. Accordingly, Applicants' effective filing date for p16 isolation, purification, and antibodies precedes the publication of Xiong et al.

In a discussion relating to antedating affidavits, MPEP 715.02 clearly states that Applicants can successfully antedate a reference by showing that they invented "no more than the reference shows" prior to the reference publication date. Applicants' priority document alone amply demonstrates prior invention by Applicants of the relevant material disclosed by Xiong et al. Accordingly, Applicants submit that Xiong et al. fails to qualify as prior art, thereby rendering this rejection moot. Reconsideration and withdrawal of this rejection are respectfully requested.

29. The Examiner suggests incorporating material from the priority documents to provide support in the present application for some embodiments of the claimed subject matter. Applicants submit that the amendments presented above incorporate sufficient material from the priority documents to fully support the subject matter of the pending claims. I state that the added material consists of the same material incorporated by reference from the priority documents.

Applicants submit herewith an amended sequence listing including SEQ ID No. 4 of the priority documents, which is presented as SEQ ID No. 35. Pursuant to the Rules, a hard copy of the sequence listing and a computer readable form of the sequence listing (the diskette) are submitted herewith. I state that this submission, filed in accordance with 37 C.F.R. §1.821(g) does not include new matter. I further state that the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. §1.821(c) and (e), respectively, are the same.

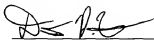
### CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

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Respectfully Submitted,



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